DOI: 10.1093/jnci/djp485
Advance Access publication on January 13, 2010.

National Institutes of Health State-of-the-Science Conference Statement: Diagnosis and Management of Ductal Carcinoma In Situ September 22–24, 2009

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Manuscript received November 5, 2009; accepted November 30, 2009.

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Foreword

National Institutes of Health consensus and state-of-the-science statements are prepared by independent panels of health professionals and public representatives on the basis of 1) the results of a systematic literature review prepared under contract with the Agency for Healthcare Research and Quality, 2) presentations by investigators working in areas relevant to the conference questions during a 2-day public session, 3) questions and statements from conference attendees during open discussion periods that are part of the public session, and 4) closed deliberations by the panel during the remainder of the second day and morning of the third. This statement is an independent report of the panel and is not a policy statement of the National Institutes of Health or the Federal Government.

The statement reflects the panel's assessment of medical knowledge available at the time the statement was written. Thus, it provides a "snapshot in time" of the state of knowledge on the conference topic. When reading the statement, keep in mind that new knowledge is inevitably accumulating through medical research.

Objective To provide health-care providers, patients, and the general public with a responsible assessment of currently available data on the diagnosis and management of ductal carcinoma in situ (DCIS).

Participants A non-Department of Health and Human Services, nonadvocate, 14-member panel representing the fields of oncology, radiology, surgery (general and reconstructive), pathology, radiation oncology, internal medicine, epidemiology, biostatistics, nursing, obstetrics and gynecology, preventative medicine and population health, and social work. In addition, 22 experts from pertinent fields presented data to the panel and conference audience.

Evidence Presentations by experts and a systematic review of the literature prepared by the Minnesota Evidence-based Practice Center, through the Agency for Healthcare Research and Quality. Scientific evidence was given precedence over anecdotal experience.

Conference process The panel drafted its statement based on scientific evidence presented in open forum and on published scientific literature. The draft statement was presented on the final day of the conference and circulated to the audience for comment. The panel released a revised statement later that day at http://consensus.nih.gov. This statement is an independent report of the panel and is not a policy statement of the National Institutes of Health or the Federal Government.

Conclusions Clearly, the diagnosis and management of DCIS is highly complex with many unanswered questions, including the fundamental natural history of untreated disease. Because of the noninvasive nature of DCIS, coupled with its favorable prognosis, strong consideration should be given to elimination of the use of the anxiety-producing term "carcinoma" from the description of DCIS. The outcomes in women treated with available therapies are excellent. Thus, the primary question for future research must focus on the accurate identification of patient subsets diagnosed with DCIS, including those persons who may be managed with less therapeutic intervention without sacrificing the excellent outcomes presently achieved. Essential in this quest will be the development and validation of accurate risk stratification methods based on a comprehensive understanding of the clinical, pathological, and biological factors associated with DCIS.

J Natl Cancer Inst 2010;102:161–169

Ductal carcinoma in situ of the breast, or DCIS, represents a spectrum of abnormal cells confined to the breast duct and is a risk factor for invasive breast cancer development. Unlike invasive breast cancer, DCIS either has not yet invaded beyond its intraductal origin or may never invade neighboring tissues. DCIS is most often diagnosed as a consequence of screening for invasive breast cancer because DCIS has no specific screening modality. The etiology of DCIS is presumably heterogeneous, making

assessment of prognosis based on pathology and imaging highly variable. On the basis of pathological and molecular studies, some DCIS represents a precursor to invasive breast cancer; however, the proportion of untreated DCIS that will progress to invasive breast cancer is unknown.

Although DCIS was first described a century ago by Dr Joseph Bloodgood, its natural history is poorly understood and is unlikely to be fully elucidated. The clinical entity, DCIS, has changed over time with the development of highly sensitive detection technologies capable of identifying breast abnormalities long before they become palpable. The earliest reports of DCIS, originally referred to as "comedo carcinoma," describe its detection either as a breast lump or as a result of abnormal discharge from the nipple. Not until the development and widespread application of mammography in the early 1980s did detection of DCIS occur primarily through mammographic screening for invasive breast cancer. Despite the relatively indolent nature of DCIS, its name includes the word "carcinoma"; therefore, its diagnosis carries a negative connotation for both patients and physicians. Because the current approaches to diagnosis and treatment of DCIS have considerable emotional and physical impact for women diagnosed, it is critical to develop risk stratification methods that enable a more precise determination of those patients who are at risk for the development of invasive disease. It is also important for the medical community to consider eliminating the term "carcinoma" in this disease, as DCIS is by definition not invasive—a classic hallmark of cancer.

With the advent of widespread screening for invasive breast cancer in the early to mid-1980s, the detection and, therefore, incidence of DCIS have increased dramatically. With the increasing prevalence of DCIS and our current inability to determine those women with DCIS who are at high risk for invasive breast cancer, it is essential that we critically evaluate the available data concerning the diagnosis and management of DCIS. Patient outcomes in DCIS trials have focused mainly on survival, local recurrence, and invasive breast cancer. The clinical significance of DCIS recurrence as an endpoint is not clear. Few data use other important outcome parameters, including patient-reported outcome measures and quality-of-life parameters. The excellent 10-year survival rates of patients who have DCIS (96%–98%) heighten the importance of these additional outcome measures. There is also a need to explore health economic issues, perform comparative effectiveness analyses, and conduct research that will result in tangible improvements in quality of life for those who have a diagnosis of DCIS.

The focus of this state-of-the-science document is to provide a summary of critically reviewed scientific data and opinions presented by experts and attendees that relate to this extraordinarily important problem. The primary challenges for the panel members in weighing the totality of this evidence have been 1) data concerning the natural history of DCIS are relatively lacking because it is usually treated by at least surgical excision as primary treatment; 2) the precise classification of DCIS has changed over time as methods to detect ever-earlier disease become available and the precision of pathological examination is enhanced through diagnostics that specifically, and with great sensitivity, identify very small numbers of malignant cells in surgical specimens; and 3) very few robust randomized clinical trials examining the various therapeutic interventions in patients with DCIS have been conducted.

This State-of-the-Science Conference, held on September 22–24, 2009, in Bethesda, Maryland, was convened by the National Cancer Institute and the Office of Medical Applications of Research of the National Institutes of Health to explore and assess the current scientific knowledge regarding the Diagnosis and Management of DCIS. For the purpose of this statement, the term DCIS refers to the complete replacement of normal ductal cells with a spectrum of abnormal cells confined to the ducts without invasion. It should be noted that the panel did not address any issues related to invasive breast cancer nor did they address lobular carcinoma in situ or atypical ductal hyperplasia (an earlier precursor in the pathway to the development of DCIS).

The key questions that the panel was asked to address were the following:

1. What are the incidence and prevalence of DCIS and its specific pathologic subtypes, and how are incidence and prevalence influenced by mode of detection, population characteristics, and other risk factors?
2. How does the use of MRI or sentinel lymph node biopsy impact important outcomes in patients diagnosed with DCIS?
3. How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?
4. In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes?
5. What are the most critical research questions for the diagnosis and management of DCIS?

During the first 2 days of the conference, experts presented information on each of the key questions. After weighing the scientific evidence, including the data presented by the speakers, input from attendees, and a formal evidence report commissioned through the Agency for Healthcare Research and Quality, an independent panel prepared and presented a draft of this State-of-the-Science Statement addressing the conference questions. The evidence report prepared for the conference is available at www.ahrq.gov/clinic/tp/dcistp.htm.

What Are the Incidence and Prevalence of DCIS and Its Specific Pathologic Subtypes, and How Are Incidence and Prevalence Influenced by Mode of Detection, Population Characteristics, and Other Risk Factors?

- DCIS incidence in the United States increased more than sevenfold from 1973 through the late 1990s and has since leveled off. The most rapid increases were among women aged 50 years and older. The current age-adjusted incidence rate of DCIS is 32.5 per 100 000 women. At age 50–64 years, the incidence is approximately 88 per 100 000. Currently, for every four diagnoses of invasive breast cancer, there is one diagnosis of DCIS. Risk of DCIS is rare in women younger than 30 years, is low in women younger than 40 years but increases steadily from age 40 to 50 years. The risk increases much more slowly after age 50 years and plateaus after age 60 years.
- As of January 1, 2005, an estimated one-half million US women were living with a diagnosis of DCIS. The prevalence is greater in white women than in black women and women of other races

and/or ethnicities. If we assume constant incidence and survival rates, it is estimated that by 2020 more than 1 million living US women will have a diagnosis of DCIS.

- The increase in rates of DCIS is highly and consistently associated with the concurrent increase in rates of mammography screening. Screening data from developed countries indicate that rates of increase and incidence of DCIS are similar to those in the United States.
- The natural history of DCIS is poorly understood. Tumor characteristics generally involve both qualitative (grade, severity, and type) and quantitative (volume) features. The qualitative features of DCIS refer to the histological pattern of ductal proliferation (spread of abnormal cells) and include the architectural pattern; high-, intermediate-, and low-grade cytological (structural) features; and the presence or absence of central necrosis (cell death). The most aggressive form is called comedo-type with high-grade cellular and nuclear features; this form is frequently associated with central necrosis and microcalcifications (small deposits of calcium). The other architectural types consist of cribriform (appearing to have open spaces or small holes), papillary (having fingerlike projections), micropapillary (having smaller fingerlike projections), and solid types. Many DCIS cases include at least two different architectural types in the same breast.
- The average tumor size of DCIS is approximately 1–1.5 cm; about one-half are high grade. The most common histological subtype is "noncomedo"; its incidence continued to increase through 2006. In contrast, the rate of the comedo subtype is much lower, peaked in 1995, and leveled off and then declined through 2006. These time trends by subtype are affected by changes in pathological reporting and coding conventions used by the Surveillance, Epidemiology, and End Results registries (www.seer.cancer.gov). Special studies are needed to establish the true rates and trends by histological subtype. Of note, Surveillance, Epidemiology, and End Results captures data on DCIS but not on atypical ductal hyperplasia (representing the part of the spectrum in the evolution of DCIS).
- Although few studies have focused on risk factors for DCIS, most suggest that the risk factors are the same as those for invasive breast cancer. These factors include high mammographic density, family history of breast cancer (eg, *BRCA* positive), increasing age, menopausal estrogen with progestin therapy, late age at menopause, nulliparity (no births), late age at first birth, and high postmenopausal body mass index.

Recommendations for Future Research. Basic descriptive epidemiology studies of DCIS, by pathological subtypes, using consistent criteria over time and across registries are needed. To facilitate this goal, we recommend that the US pathology community adopt national standardized reporting of DCIS.

How Does the Use of MRI or Sentinel Lymph Node Biopsy Impact Important Outcomes in Patients Diagnosed With DCIS?

Magnetic resonance imaging (MRI) and sentinel lymph node biopsy are two diagnostic techniques that can be used to inform the management of patients who have DCIS. MRI is increasingly used in the pretreatment evaluation of patients who have DCIS to determine the local extent of the known DCIS, identify multicentric tumors, and evaluate for disease in the contralateral breast. Sentinel lymph node biopsy is a surgical procedure to remove the lymph node that first receives drainage from the tumor site. Sentinel lymph node biopsy has largely replaced routine axillary lymph node dissection for staging invasive breast cancer because it is less invasive and has lower associated morbidity while preserving diagnostic accuracy. For the majority of women who have DCIS treated with excision, sentinel lymph node biopsy is not necessary. Sentinel lymph node biopsy may be considered at the time of mastectomy because there is a chance that invasive cancer will be found in the specimen, and once a mastectomy has been done, there is no longer an opportunity to perform sentinel lymph node biopsy. Involvement of the axillary lymph node influences treatment decisions and prognosis. A number of unanswered questions exist about the risks and benefits of using these two diagnostic techniques in patients who have DCIS, particularly as they relate to important outcomes, such as the recurrence of DCIS, progression of DCIS to invasive cancer, patient quality of life, and overall survival.

What We Know About MRI in DCIS. Historically, breast MRI has been used in two primary applications: for early detection in individuals at high risk of breast cancer and to further evaluate patients who have a current breast cancer diagnosis. There is now increasing use of MRI in DCIS. Progress in diagnostic MRI has been made over the past decade, owing to several advances that have improved the imaging's spatial resolution and increased contrast differentiation between normal and abnormal breast tissue.

For DCIS, most studies have found that MRI is more sensitive than mammography for detecting multicentric disease; however, limited data exist on the specificity of MRI in this setting. The results of studies comparing MRI with mammography and pathological evaluation for determining the size of a DCIS are inconsistent. Overall, MRI is believed to slightly improve on mammography but has been found to both underestimate and overestimate the size of DCIS lesions relative to pathological analysis. Importantly, the ways in which surgically resected breast tissues are processed can limit the accuracy of pathologically based tumor measurements as well. MRI also is used to detect occult DCIS or breast cancer in the contralateral breast but can result in false-positive and false-negative results.

What We Need To Know About MRI in DCIS. A number of questions remain about the use of MRI in DCIS. To what degree does the improved sensitivity of breast MRI inform treatment decisions, and how does MRI affect the rates of breast biopsy, local excision, local excision with radiotherapy, and mastectomy? Beyond management concerns, we do not know how MRI influences outcomes such as recurrence of DCIS or invasive breast cancer or independent effects of MRI interpretation on patient anxiety and patient quality of life. Given that the majority of treated DCIS lesions will not progress to invasive breast cancer, to what degree does breast MRI in this setting result in overdetection, meaning the detection of biologically insignificant lesions. What are the psychological, physical, and medical costs associated with MRI-based overdetection, and do barriers to access to the technology exist? Finally, can

we identify MRI features that can be combined with clinical and biological characteristics to better stratify risk in patients who have DCIS?

What We Know About Sentinel Lymph Node Biopsy in DCIS. Sentinel lymph node biopsy is reasonable in women undergoing mastectomy for DCIS. The value of sentinel lymph node biopsy in DCIS depends on the incidence of sentinel lymph node metastasis. The incidence of sentinel lymph node metastasis in patients with an excisional diagnosis of DCIS is approximately 5%. These pooled data are limited because different studies have blurred the distinctions between pure DCIS and DCIS with microinvasion. Similarly, positive sentinel lymph node metastases are inconsistently defined. Moreover, the clinical significance of positive sentinel lymph node metastases in patients who have DCIS is indeterminate, given that the majority of them are micrometastases or isolated tumor cells. Existing studies of sentinel lymph node biopsy have been reported in highly selected patient populations that may not represent the general population of women who have DCIS. Studies of the impact of sentinel lymph node biopsy for DCIS on subsequent treatments have been limited to descriptions of single, not multicenter, practices. Finally, although sentinel lymph node biopsy is less invasive than axillary lymph node dissection, multiple studies have shown that sentinel lymph node biopsy is associated with some risk of complications, including lymphedema (swelling that most often occurs in the limbs; about 3%), impaired shoulder movement (about 3%), arm or shoulder pain (about 8%), and numbness (about 12%).

What We Need To Know About Sentinel Lymph Node Biopsy in DCIS. Although roughly 5% of patients with an excisional diagnosis of DCIS are found to have positive sentinel lymph node biopsy results, uncertainty still remains about the clinical significance of isolated tumor cells or micrometastases in the lymph nodes. As well, it is not clear what role sentinel lymph node biopsy plays in DCIS with microinvasion. Studies are needed to determine the effects of sentinel lymph node biopsy for DCIS on the important outcomes of recurrence of DCIS or invasive cancer and patient quality of life.

Recommendations for Future Research.

- Determine the comparative effectiveness of MRI with regard to the management of DCIS, particularly surgical management, following diagnostic biopsy.
- Evaluate and improve breast MRI techniques to enable discrimination between DCIS that requires intervention and DCIS that may be managed with active surveillance.
- Determine the prognostic significance of sentinel lymph node micrometastases in DCIS.

How Do Local Control and Systemic Outcomes Vary in DCIS Based on Tumor and Patient Characteristics?

- DCIS does not recur systemically in the vast majority of women who are treated. Because of the low mortality rates, the primary outcomes of DCIS studies focus on the development of a local recurrence of DCIS or invasive breast cancer. Recurrence as an adverse outcome in many studies has not been consistently defined. Features associated with a higher risk of local recurrence or progression to invasive disease are patient characteristics, such as young age, race, symptomatic presentation, and tumor characteristics, such as high nuclear grade, "comedo-type" necrosis, and tumor size. For women undergoing local excision, the width of the resection margin is also critical to prognosis.

What We Know.

Patient characteristics.

- Numerous studies, including randomized controlled trials, show a consistent association between younger age at diagnosis and an increased risk for adverse outcomes. These studies also demonstrate poorer outcomes among women whose DCIS was detected by symptoms compared with women whose DCIS was detected by screening mammography alone. In addition, several studies—including one analysis of more than 15 years of Surveillance, Epidemiology, and End Results data (1988–2003)—demonstrate higher breast cancer mortality and recurrence rates among black women who have DCIS compared with white women who have DCIS. These differences persisted after controlling for differences in age, tumor characteristics, and treatment but not for differences in screening rates or mode of presentation. Keeping in mind the overall high survival rates for DCIS, the absolute difference in mortality is small, but the differences in race should be confirmed through further investigation. The prognostic impact of other risk factors, such as reproductive factors and mammographic density, also warrant further study.

Tumor characteristics.

- An understanding of the tumor biology of DCIS is needed to determine the invasive tendency, recurrence probabilities, and response to therapy. Our current knowledge is limited to the identification of surrogate markers for clinical behavior and outcome. Tumor characteristics associated with recurrence and progression to invasive carcinoma include the microscopic features of the tumor, the topographic nature (size, location, and extent) of the tumor, and the adequacy of its surgical resection.
- High-grade DCIS, and the architectural pattern of "comedo-type" necrosis are strongly associated with local recurrence and progression to invasive carcinoma. The finding of microinvasive carcinoma associated with DCIS is a predisposing risk factor for recurrence and dissemination. DCIS that is extensive in distribution, is large in size, or involves the surgical resection margin is associated with a high likelihood for local recurrence. Wider surgical margins are associated with a decreased risk of local recurrence, but controversy exists as to the optimal margin size.
- Studies of molecular characteristics demonstrate that the presence of estrogen receptors in DCIS is associated with a reduction in the risk of ipsilateral (same breast) recurrence. However, these studies have not simultaneously investigated the impact of tumor grade. Evidence about other molecular markers is insufficient to stratify prognostic groups. The combination of prognostic tumor factors is likely to be more informative than single factors used in isolation.

What We Need To Know.

- Despite available research, we are still unable to identify accurately which patients with DCIS will progress to invasive breast cancer and how to prevent this progression altogether. There is a lack of reliable models representing human DCIS to support the comprehensive investigations needed to evaluate cellular and molecular alterations in the epithelium and microenvironment (surrounding area).

Recommendations for Future Research Directions.

- Efforts need to be directed toward improving the diagnostic accuracy and reproducibility of DCIS classification and grading schemes.
- Research should focus on the molecular events and pathological and radiographic features governing the progression of DCIS to enable an understanding of the relationship between tumor biology and clinical outcomes.
- Combinations of new and existing clinical, pathological, and molecular factors should be investigated and validated to better risk-stratify patients who have DCIS. Ease of utilization, predictive ability, reproducibility, and generalizability are important components of research on prognostic models.
- Additional research evaluating the reproducibility of one study that indicated a racial disparity in mortality among black women who have DCIS (compared with white women who have DCIS) is needed.

In Patients With DCIS, What Is the Impact of Surgery, Radiation, and Systemic Treatment on Outcomes?

- DCIS is a heterogeneous disease associated with high rates of long-term, disease-free survival (96%–98%) when treated with currently available therapies. It is unclear whether all patients who have DCIS uniformly benefit from these interventions. Given the lack of clarity and the incomplete data surrounding the natural history, prognostic factors, and biology of DCIS, important therapeutic questions remain unanswered.
- One major question relates to the impact of tumor and stromal biology on therapeutic choices (ie, treatment vs no treatment or radiotherapy vs no radiotherapy) and on patient outcomes. The interaction of host factors with the biology of the tumor is poorly understood in DCIS patients. Identifying predictive and prognostic biomarkers that are reflective of biology would better inform therapeutic decision making and should be a research priority.
- Better decision-making tools are needed to aid patients and their care providers in choosing among therapeutic options. Patients experience anxiety related to the diagnosis of DCIS, the complexity of decision making, and misperceptions regarding outcomes and risks of therapy. Women who have DCIS should have access to the best-available information and guidance to help make decisions about their care that reflect their personal circumstances and preferences. Therefore, these issues should be incorporated within the construction and validation of decision-making tools. Economic issues and the accessibility and quality of care also should be studied.

What We Know.

- Mastectomy and local excision with radiotherapy are both effective local therapeutic approaches in patients who have DCIS. A randomized controlled trial comparing mastectomy with local excision and radiation has not been done, but current data demonstrate that long-term survival is similar with either approach. Although survival rates are similar, there is a higher local recurrence risk for DCIS with local excision and radiation therapy (12%, half of whom have invasive cancer) than in patients who choose mastectomy (about 1%).
- Randomized clinical trials show that radiotherapy after local excision reduces the risk of both invasive and noninvasive local recurrence, compared with local excision alone, with equivalent survival.
- Tamoxifen is currently the only Food and Drug Administration–approved systemic agent for preventing local recurrence in patients who have DCIS. Evidence demonstrates a benefit of tamoxifen in estrogen receptor–positive DCIS. In randomized clinical trials, tamoxifen has been shown to reduce the risk of invasive cancer in the ipsilateral and contralateral breasts, but no survival benefit has been shown. There is currently no defined role for raloxifene in patients who have DCIS. There is no role for chemotherapy in patients who have pure DCIS.

What We Need To Learn.

- The risk of DCIS in the contralateral breast is generally low. Although women are increasingly choosing prophylactic mastectomy of the contralateral breast, no clear data exist to suggest that this improves outcomes. The reasons for this increase require further study.
- Randomized clinical trials demonstrate that all subsets of patients benefit from radiotherapy in terms of decreased local recurrence. However, there may be a subgroup of women who have DCIS in which the risk of local recurrence is so low that radiotherapy may be of no benefit. In addition, there also may be a subset of women who can be monitored after biopsy in lieu of surgery or other therapies. Tumor size, margin status, biological factors, age, comorbidities, patient preference, grade, and mammographic density may all be relevant factors in such decision making. The favorable long-term survival rate in DCIS justifies the initiation of clinical trials to risk-stratify patients to determine whether these patient subsets exist.
- The presence of a positive margin increases the risk of local recurrence. Some retrospective data suggest that larger margins are associated with a lower risk of local recurrence. For those patients who elect to have local excision without radiotherapy, an optimal margin size needs to be established. Standardization of procedures, such as specimen handling and margin assessment, is crucial to the implementation of trials investigating this issue.
- Despite appropriate therapy with local excision and radiotherapy, women who have DCIS continue to have a defined risk of recurrent DCIS and invasive breast cancer years after treatment. Retrospective studies suggest that the inclusion of a radiation boost to the excisional cavity is associated with a reduced risk of local recurrence of DCIS or invasive disease.
- If radiotherapy is used, whole-breast radiotherapy is the standard technique, although accelerated partial-breast radiotherapy is being studied in ongoing clinical trials. Investigation of partial-breast radiotherapy and accelerated radiotherapy regimens is an appropriate focus of clinical research.

- The role of other hormonal therapies in patients who have DCIS is unknown. We await the results of a recently closed randomized clinical trial comparing aromatase inhibitors with tamoxifen for prevention of recurrence in women who have DCIS and have undergone local excision therapy. Targeted molecular therapies also are being evaluated in patients who have DCIS and have undergone local excision with radiation.
- It is important to stress that DCIS has a high probability of long-term disease-free survival and that all current therapies have short- and long-term side effects. Therefore, future therapeutic research efforts should focus on the identification of patients who are at high risk for developing recurrence. Such identification through the appropriate investigation of biomarkers could be helpful in guiding both systemic and local therapy decisions. Biomarker discovery also may aid in the development of novel, less toxic, targeted agents for this population of patients.

Recommendations for Future Research Directions.

- Develop and validate risk stratification models to identify subsets of women with DCIS who are candidates for 1) active surveillance only, 2) local excision only, 3) local excision with radiotherapy, and 4) mastectomy.
- Develop strategies to determine which patient is at high risk for recurrence of DCIS or the development of invasive carcinoma.
- Perform comparative effectiveness analyses to further define the role of current therapies in DCIS patients.
- Integrate patient-reported outcomes and data on patient perceptions of risk and preferences regarding treatment within current clinical research and, ultimately, decision-making algorithms.

What Are the Most Critical Research Questions for the Diagnosis and Management of DCIS?

In summary, we have identified the following major areas as critical in the advancement of our understanding of DCIS:

1. Development and use of standardized reporting methods and terminology for DCIS detection and diagnosis across all disciplines.
2. Collection of consistent and detailed data on the clinical, pathological, radiological, and molecular characteristics of DCIS through the creation of multisite databases of DCIS that would include annotated specimen and imaging repositories.
3. Investigation and validation of combinations of new and existing clinical, radiological, pathological, and molecular factors to improve risk stratification of DCIS patients and thus to identify the optimal therapy for each individual. Ease of use, predictive ability, reproducibility, and generalizability are important components of prognostic model development.
4. Research on patient–provider communication, informed consent (at the time of screening), patient preferences, and decision making concerning the diagnosis and treatment of DCIS. Decision aids should be further developed, evaluated for their impact on quality of care, and integrated into clinical practice.
5. Investigations of the impact a diagnosis and treatment of DCIS has on the quality of life.
6. Investigations into the comparative effectiveness of the methods of treatment for DCIS.

Conclusions

The diagnosis and management of DCIS is highly complex with many unanswered questions, including the fundamental natural history of untreated disease. Because of the noninvasive nature of DCIS, coupled with its favorable prognosis, strong consideration should be given to remove the anxiety-producing term "carcinoma" from the description of DCIS. The outcomes in women treated with available therapies are excellent. Thus, the primary question for future research must focus on the accurate identification of patient subsets diagnosed with DCIS, including those persons who may be managed with less therapeutic intervention without sacrificing the excellent outcomes presently achieved. Essential in this quest will be the development and validation of accurate risk stratification methods based on a comprehensive understanding of the clinical, radiological, pathological, and biological factors associated with DCIS.

Appendix 1

Consensus Development Panel

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Planning Committee members provided their input at a meeting held January 13–15, 2008. The information provided here was accurate at the time of that meeting.

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Note

The Consensus Development Panel members, Speakers, Planning Committee, Conference Sponsors, Conference Cosponsor, and Conference Partners are given in Appendix 1.

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